Discussion: UHR-P showed significant cortical thinning in several regions of the right cingulate cortex in comparison to HC, giving support to the notion that structural alterations in the cingulate cortex may be present in children and adolescents prior the onset of psychosis. Longitudinal changes in CTH have the potential to increase understanding of changes related to transition to clinical illness.

T175. A 10-YEAR LONGITUDINAL STUDY OF GREY MATTER VOLUME IN FIRST EPISODE OF NON-AFFECTIVE PSYCHOSIS

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Background: Structural abnormalities in First Episode of Non- Affective Psychosis (FEP) are shown to be present at the time of onset of the illness. Although there are multiple cross-sectional studies in chronic patients there is no clear evidence how these alterations progress years after the appearance of the first episode.
Methods: Data for the present investigation were obtained from an ongoing epidemiological and longitudinal intervention programme of first-episode psychosis (PAFIP) conducted at the Marqués de Valdecilla University Hospital (HUMV), Spain. Images for 62 FEP patients and 47 healthy controls were acquired at baseline and 10 year follow-up on the same 1.5-T whole-body scanner (SIGNA, GE, Milwaukee, WS, USA). Three-dimensional T1-weighted images, using a spoiled gradient-recalled acquisition in the steady state (GRASS) (SPGR) sequence, were acquired in the coronal plane with the following parameters: TE=5 msec, TR =24 msec, NEX=2, rotation angle =45°, FOV= 26 x 19.5 cm, slice thickness =1.5 mm and a matrix of 256 x 192.
Structural imaging data for each subject was analyzed using serial longitudinal Statistical Parametric Mapping software (SPM12). After segmenting the mid-point average and multiply the result by the jacobian maps, DARTEL was applied to spatially normalise de diferences. T-test between both groups was performed, allowing voxel-wise comparison of progressive structural change. All results were p<0.05 FWE corrected.
Results: FEP patients exhibited progressive bilateral atrophy of the anterior cingulate bilaterally, the right inferior orbital, middle and superior frontal giri, left precentral and postcentral giri and cerebellum. We found no areas were grey matter was greater in controls than in patients.
Discussion: In this study we analyze a well characterized sample of patients with a first episode of non-affective psychosis in the first weeks after onset and 10 years later. Our results confirm that, apart from the grey matter volume reduction presented at baseline, patients show a progressive grey matter loss in anterior cingulate, frontal and parietal lobes as well as cerebellum.

T176. REDUCED WHITE MATTER 'CONNECTIVITY' IN THE SPLENIUM OF THE CORPUS CALLOSUM IN TREATMENT-RESISTANT SCHIZOPHRENIA

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Background: Resistance to treatment affects up to 30% of patients with schizophrenia (SCZ). Current criteria for treatment-resistant schizophrenia (TRS) require failure to respond to two antipsychotic trials for adequate dose and duration. Clozapine is the only antipsychotic that is more effective to treatment resistant patients. Increasing evidence suggest that TRS may represent a subgroup of patients with distinct biological signature. Brain dysconnectivity was proposed as a major feature of schizophrenia and more intense in TRS patients. Earlier identification of TRS may anticipate the clozapine trial and, thus, reduce disability and treatment costs. In our study, we investigated whether there were differences in white matter integrity among first episode of psychosis (FEP), treatment-resistant schizophrenia (TRS), and non treatment-resistant schizophrenia (NTRS) patients.
Methods: Diffusion-tensor brain MRI images were obtained for 34 TRS (19 males), 50 NTRS (26 males) and 35 FEP individuals (18 males), on a Siemens 1.5T MRI scanner. Treatment resistance was defined as persistence of moderate to severe symptoms, after failure to respond to 4–6 week trials of at least two different antipsychotic medications in adequate doses (equivalent to at least 400 mg/day of chlorpromazine or 5 mg/day of risperidone). All participants were receiving antipsychotic medication. All TRS patients were in clozapine use. Analysis of diffusion parameters was performed using a tract-based spatial statistics (TBSS), yielding a total two contrasts: i) mean FA is lower (or higher) in the TRS compared to the FEP, ii) mean FA is lower (or higher) in the NTRS compared to the FEP corrected for multiple comparisons using family-wise error (FWE) < 0.05. Gender and age were used as covariates.
Results: FEP patients were younger than TRS (mean±SD; 27.2 ± 7.93 y/o vs 37.06 y ±7.98 y/o;t=5.08, p <0.001) and NTRS (27.2 ± 7.93 y/o vs 37.71 y ±11.18 y/o; t=4.57, p<0.001) patients. Reduced in FA value was observed in the splenium of the corpus callosum (CC) in TRS patients when compared to FEP (47,598 voxels and thresholded at p<0.05). No differences between NTRS and FEP patients were observed.
Discussion: Our results showed reduced FA value in the splenium of the CC in TRS when compared to FEP. The splenium of corpus callosum connects the temporal and occipital cortices, and have been previously associated with schizophrenia, but not specifically to treatment resistance in schizophrenia. Our data might suggest that patients with resistance to treatment have inefficiency in the connectivity of the white matter between these regions. Further studies will be required to replicate these findings and to explore the significance of white matter changes in the brain in order to determine if these are consequence of disease progression or related to clozapine exposure.

T177. STRUCTURAL ORGANIZATION OF THE PRAXIS NETWORK PREDICTS GESTURE PRODUCTION: EVIDENCE FROM HEALTHY SUBJECTS AND PATIENTS WITH SCHIZOPHRENIA

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Background: Hand gestures are an integral part of social interactions and are involved in nonverbal and verbal communication. The convey language that is expressed by motor actions, and thus depend on the interplay of various brain regions. Several functional magnetic resonance imaging studies in healthy subjects suggest the praxis network for gesture production, involving distinct frontal, parietal and temporal regions. Lesions studies in subjects with apraxia, following left brain damage corroborate these findings. However, little is known about the structural connectivity underlying gesture production. We aimed to provide novel insights into the structural connectivity of the praxis network and how it is related to gesture production.
Methods: Our sample consisted of 41 healthy subjects and of 40 patients with schizophrenia, demonstrating gesture impairments and structural network abnormalities. All participants performed a gesture production test, the test of upper limb apraxia and underwent diffusion weighted magnetic resonance imaging. Finsler geometry was used to investigate structural connectivity and graph theory to estimate global and local efficiency of the praxis network, which consists of 13 bilateral regions of interest.
Results: Our findings showed an association of gesture production with network attributes and specific connections within the praxis network. Thus, global and local efficiency and most of the intra- and interhemispheric connections within the gesture network predicted gesture production across groups. Global efficiency of the praxis network further predicted gesture production only in the patient group. Local efficiency of many ROIs and connections of interest predicted production in patients at trend-level. In contrast, there were no significant or trend-level associations of gesture production with network attributes in controls.
Discussion: The results revealed an association of impaired gesture performance with structural alterations of the praxis network, including global and local efficiency and many connections of interest. Our findings are of great importance in the understanding of the structural correlates of gesture production and shed further light on the neural underpinnings of gesture deficits in a patient group with severe social deficits.

T178. PRIOR SUB-THRESHOLD PSYCHOTIC SYMPTOMS ASSOCIATED WITH THICKER RIGHT INFERIOR FRONTAL GYRUS AMONG PATIENTS IN A FIRST EPISODE OF PSYCHOSIS

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Background: Individuals with attenuated or sub-threshold psychotic symptoms (STPS) are considered at-risk for psychosis. The notion that STPS represent "early psychosis" holds promise as it suggests the possibility of charting the developmental course of psychotic illness with neuroimaging. However, recent evidence suggests that a significant minority of patients in a first episode of psychosis (FEP) do not recall pre-onset STPS, suggesting diversity in early positive symptom course. This diversity may be reflected at the level of neurodevelopment. While imaging studies of at-risk youth and FEP patients reveal progressive trends in cortical thinning across stages of illness, none have considered the STPS history of FEP patients. To better understand neurobiological trends across illness stages, we investigate the relationships between STPS history and cortical thickness in FEP patients using a whole-brain approach.
Methods: Patients (N=93) were recruited from a specialized early intervention clinic for FEP at the Douglas Mental Health University Institute. The Circumstances of Onset and Relapse Schedule was administered to identify youth who recalled at least one of nine expert-selected STPS prior to their FEP (STPS+, N=67) compared to those who did not (STPS-, N=26). These STPS include: Suspiciousness or odd ideas of reference, odd or bizarre ideas that are not delusional, unusual or eccentric behavior, unusual perceptual experiences that are not clearly psychotic, disorganized or odd speech, inappropriate affect, hallucinations or delusions (sub-threshold), and passivity experiences. Age and sex-matched healthy controls were recruited (N=83) for comparison. Participants were scanned on a 1.5T MRI scanner between 1 and 3 times at baseline, at 1-year follow-up, and at 2-year follow-up. Structural T1-weighted images were processed through the CIVET 2.1 pipeline. Cortical thickness values of 320 scans (143 HC, 123 STPS+, 54 STPS-) that passed quality control were extracted for group analysis. Linear mixed effects models controlling for effects of age, sex, education, and mean whole-brain thickness were applied to obtain vertex-wise F-test maps comparing groups.
Results: Post-hoc vertex-wise t-test maps were thresholded with Random Field Theory (p-cluster=0.001) and revealed that compared to controls, only STPS- patients exhibited significantly thinner cortical thickness in the right inferior frontal gyrus (peak $t(162.3)=4.13$, $p<0.001$). Examination of mean cortical thickness within this cluster, comparing patient groups only, revealed that compared to STPS+ patients, STPS- patients exhibited significantly thinner cortical thickness ($t(172)=-2.55$, $p=0.01$). This difference was most pronounced at baseline.
Discussion: These results indicate that within the right prefrontal cortex, STPS+/- patients may undergo different cortical maturation trajectories leading up to and through a first episode of psychosis. These differences may explain differential vulnerability to sub-threshold psychotic symptomology before a full-blown episode. In addition to suggesting differential underlying neurobiology related to STPS, these results suggest the importance of considering STPS history in mapping the trajectories of cortical thickness among FEP patients.

T179. DO INDIVIDUALS IN A CLINICAL HIGH-RISK STATE FOR PSYCHOSIS DIFFER FROM HEALTHY CONTROLS IN THEIR CORTICAL FOLDING PATTERNS?

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Background: Volumetric brain differences between persons meeting criteria for a clinical high-risk state for psychosis (CHR) and healthy controls (HC) have been previously reported, yet little is known about potential abnormalities in surface-based morphological measures. Gyrification (i.e., the amount of cortical convolution) remains relatively stable across the lifespan and is minimally influenced by ubiquitous confounding factors (e.g., drug use, medication, or stress). Recently, a multi-site analysis conducted in 104 CHR persons found global increases in cortical gyrification compared to HC (Sasabayashi et al. 2017). If replicated, gyrification abnormalities in CHR could potentially serve as early neuromarkers of elevated risk, and thus could eventually be used to identify objectively and efficiently the CHR state.
Methods: A total of 124 CHR and 264 HC subjects were recruited as part of the PRONIA consortium (www.pronia.eu), a large-scale international longitudinal study currently consisting of 10 European sites. Cortical surfaces were reconstructed from structural MRI images using a volume-based, newly introduced technique called the Projection-Based-Thickness (PBT) as available in the SPM-based-toolbox CAT12. Local gyrification was quantified automatically across the whole brain as absolute mean curvature for each vertex of the brain surface mesh consisting of thousands of individual measurement points. Vertex-wise differences of curvature values were calculated applying a General Linear Model, corrected for age, gender and site effects. Results were investigated at corrected and uncorrected levels.